SEQUENCE LISTING

- <110> Allan, Bernard
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 Lavan, Brian
 Moodie, Shonna
 Waters, Steve
 Wong, Chi-Wai
 Metabolex, Inc.
- <120> Methods of Diagnosing and Treating Diabetes and Insulin Resistance
- <130> 016325-014000US
- <140> US 10/516,399
- <141> 2005-01-26
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Arg Pro Leu Trp Glu Gln Val Gln Gly Phe Arg Glu Ala Val Pro
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Gly Gly Leu Val Cys Arg Ala Leu Leu Ser Val Met Asp Asp His Asn
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Val Asp Ser Phe Ile Ser Leu Ser Ser Pro Gln Met Gly Gln Tyr Gly
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Tyr Leu Arg Asp Ser Phe Gly Leu Lys Thr Leu Leu Ala Arg Gly Ala
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Ser Tyr Ser Phe Arg His Leu Leu Asp Tyr Ile Asn Glu Thr His Thr 50 55 60

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Val Asp Ser Phe Ile Ser Leu Ser Ser Pro Gln Met Gly Gln Tyr Gly 130 135 140

Asp Thr Asp Tyr Leu Lys Trp Leu Phe Pro Thr Ser Met Arg Ser Asn 145 150 155 160

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Ala Trp Arg Lys Asn Phe Leu Arg Val Gly Arg Leu Val Leu Ile Gly 210 220

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Phe Gly Leu Gly Leu Leu Arg Ser Lys Gln Ile Lys Arg Met Ile 105 110

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Lys Ile Met Ala Pro Val Tyr Phe Ile Leu Gly Gly Lys Lys Ser Gly 275 280 285

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390

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Lys Glu Lys	Val Lys 725	Lys I	Lys Glu	Lys	Lys 730	Gln	Glu	Glu	Glu	Glu 735	Thr
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- Leu Ala Ser Arg Gly Gln Glu Pro Thr Lys Ser Lys Thr Lys Gly Asn 1060 1065 1070
- Asp Phe Phe Ile Asp Asp Ser Lys Leu Ala Ser Ala Asp Asp Ile Gly
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- Thr Thr Thr Val Thr Lys Leu Ser Thr Pro Ser Thr Gly Gly Ser 1490 1495 1500
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- Thr Val Thr Asp Ser Leu Thr Thr Gly Gly Thr Leu Val Thr Ser 1525 1530 1535
- Met Thr Val Ser Lys Glu Tyr Ser Thr Arg Asp Lys Val Lys Leu Met 1540 1545 1550
- Lys Phe Ser Arg Pro Lys Lys Thr Arg Ser Gly Thr Ala Leu Pro Ser 1555 1560 1565
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- Tyr Pro Ser Pro Arg Pro Thr Phe Gly Ile Thr Trp Arg Tyr Arg Leu 1620 1625 1630
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Gly Ser Asn Gly Lys Thr Tyr Leu Asn His Cys Glu Leu His Arg Asp
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Ala Cys Leu Thr Gly Ser Lys Ile Gln Val Asp Tyr Asp Gly His Cys
Lys Glu Lys Lys Ser Ala Ser Pro Ser Ala Ser Pro Val Val Cys Tyr
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                                                    110
Gln Ala Asn Arg Asp Glu Leu Arg Arg Leu Ile Gln Trp Leu Glu
                            120
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Ala Glu Ile Ile Pro Asp Gly Trp Phe Ser Lys Gly Ser Asn Tyr Ser
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Glu Ile Leu Asp Lys Tyr Phe Lys Ser Phe Asp Asn Gly Asp Ser His
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                                        155
Leu Asp Ser Ser Glu Phe Leu Lys Phe Val Glu Gln Asn Glu Thr Ala
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                                    170
Ile Asn Ile Thr Thr Tyr Ala Asp Gln Glu Asn Asn Lys Leu Leu Arg
                                185
Ser Leu Cys Val Asp Ala Leu Ile Glu Leu Ser Asp Glu Asn Ala Asp
                            200
Trp Lys Leu Ser Phe Gln Glu Phe Leu Lys Cys Leu Asn Pro Ser Phe
                        215
                                             220
Asn Pro Pro Glu Lys Lys Cys Ala Leu Glu Val Glu Thr Tyr Ala Asp
225
Gly Ala Glu Thr Glu Val Asp Cys Asn Arg Cys Val Cys Ser Cys Gly
                                    250
His Trp Val Cys Thr Ala Met Thr Cys Asp Gly Lys Asn Gln Lys Gly
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Gln Lys His Gln Gly Thr Ala Glu Lys Thr Lys Lys Val Asn Thr Lys
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Glu Ile
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gaggaacaaa gaagcaaatc caagatctgc gccaatgtgt tttgtggagc tggccgggaa 180
tgcgccgtca cggagaaggg ggagccaacg tgcctctgca ttgagcaatg caaacctcac 240
aagaggcctg tgtgtggcag taatggcaag acctacctca accattgtga acttcacaga 300
gacgcctgcc tcactggatc caagatccag gttgattatg atgggcactg caaagaaaag 360
aagtetgtga gteeateege cageeeegtt gtetgetate aggetaaceg tgatgagetg 420
cggcgccgga tcatccagtg gctggaagcc gagatcattc cagatggctg gttctctaaa 480
ggcagtaact acagtgagat cctagacaag tactttaaga gctttgataa tggtgactct 540
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accgcttacc ccaatcagga gaacaacaaa ctgctcagag gcctctgtgt tgatgccctc 660
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ctcaacccat ccttcaaccc tcctgagaag aagtgcgccc tggaggacga aacctatgca 780
gatggagctg agaccgaggt ggactgcaat cgctgtgtct gttcctgtgg acactgggtc 840
tgcacagcga tgacctgtga tggaaagaat cagaaggggg tccagaccca cacagaggag 900
gagatgacga gatatgccca ggaactccag aagcaccagg gaacagcaga aaagaccaag 960
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Phe Cys Gly Ala Gly Arg Glu Cys Ala Val Thr Glu Lys Gly Glu Pro
Thr Cys Leu Cys Ile Glu Gln Cys Lys Pro His Lys Arg Pro Val Cys
Gly Ser Asn Gly Lys Thr Tyr Leu Asn His Cys Glu Leu His Arg Asp
                                         75
                    70
65
Ala Cys Leu Thr Gly Ser Lys Ile Gln Val Asp Tyr Asp Gly His Cys
Lys Glu Lys Lys Ser Val Ser Pro Ser Ala Ser Pro Val Val Cys Tyr
            100
                                105
                                                    110
Gln Ala Asn Arg Asp Glu Leu Arg Arg Ile Ile Gln Trp Leu Glu
                            120
Ala Glu Ile Ile Pro Asp Gly Trp Phe Ser Lys Gly Ser Asn Tyr Ser
                        135
                                            140
Glu Ile Leu Asp Lys Tyr Phe Lys Ser Phe Asp Asn Gly Asp Ser His
Leu Asp Ser Ser Glu Phe Leu Lys Phe Val Glu Gln Asn Glu Thr Ala
                                    170
Val Asn Ile Thr Ala Tyr Pro Asn Gln Glu Asn Asn Lys Leu Leu Arg
                                                    190
            180
                                185
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Gly Leu Cys Val Asp Ala Leu Ile Glu Leu Ser Asp Glu Asn Ala Asp
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Trp Lys Leu Ser Phe Gln Glu Phe Leu Lys Cys Leu Asn Pro Ser Phe
Asn Pro Pro Glu Lys Lys Cys Ala Leu Glu Asp Glu Thr Tyr Ala Asp
                                        235
Gly Ala Glu Thr Glu Val Asp Cys Asn Arg Cys Val Cys Ser Cys Gly
                                    250
His Trp Val Cys Thr Ala Met Thr Cys Asp Gly Lys Asn Gln Lys Gly
Val Gln Thr His Thr Glu Glu Met Thr Arg Tyr Ala Gln Glu Leu
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Gln Lys His Gln Gly Thr Ala Glu Lys Thr Lys Lys Val Asn Thr Lys
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Glu Ile
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Lys Ala Tyr Glu Val Arg Ile Lys Met Val Ala Val Gly Ile Cys Arg
                             40
        35
Thr Asp Asp His Val Val Ser Gly Asn Leu Val Thr Pro Leu Pro Val
Ile Leu Gly His Glu Ala Ala Gly Ile Val Glu Ser Val Gly Glu Gly
                     70
Val Thr Thr Val Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Thr Pro
Gln Cys Gly Lys Cys Arg Val Cys Lys Asn Pro Glu Ser Asn Tyr Cys
                                105
                                                    110
Leu Lys Asn Asp Leu Gly Asn Pro Arg Gly Thr Leu Gln Asp Gly Thr
Arg Arg Phe Thr Cys Arg Gly Lys Pro Ile His His Phe Leu Gly Thr
                        135
Ser Thr Phe Ser Gln Tyr Thr Val Val Asp Glu Asn Ala Val Ala Lys
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145

Ile Asp Ala Ala Ser Pro Leu Glu Lys Val Cys Leu Ile Gly Cys Gly 170 Phe Ser Thr Gly Tyr Gly Ser Ala Val Asn Val Ala Lys Val Thr Pro Gly Ser Thr Cys Ala Val Phe Gly Leu Gly Gly Val Gly Leu Ser Ala Val Met Gly Cys Lys Ala Ala Gly Ala Ala Arg Ile Ile Ala Val Asp 215 Ile Asn Lys Asp Lys Phe Ala Lys Ala Lys Glu Leu Gly Ala Thr Glu Cys Ile Asn Pro Gln Asp Tyr Lys Lys Pro Ile Gln Glu Val Leu Lys 250 Glu Met Thr Asp Gly Gly Val Asp Phe Ser Phe Glu Val Ile Gly Arg Leu Asp Thr Met Met Ala Ser Leu Leu Cys Cys His Glu Ala Cys Gly 280 Thr Ser Val Ile Val Gly Val Pro Pro Ala Ser Gln Asn Leu Ser Ile 290 295 Asn Pro Met Leu Leu Thr Gly Arg Thr Trp Lys Gly Ala Val Tyr Gly Gly Phe Lys Ser Lys Glu Gly Ile Pro Lys Leu Val Ala Asp Phe Met Ala Lys Lys Phe Ser Leu Asp Ala Leu Ile Thr His Val Leu Pro 345 Phe Glu Lys Ile Asn Glu Gly Phe Asp Leu Leu His Ser Gly Lys Ser 360 355 Ile Arg Thr Val Leu Thr Phe 370 <210> 45 <211> 1128 <212> DNA <213> Mus musculus <223> mouse alcohol dehydrogenase (ADH2) cDNA <220> <221> CDS <222> (1)..(1128) <223> ADH2 <400> 45 atgagcactg cgggaaaagt gatcaaatgc aaagctgcgg tgctatggga gcttcacaaa 60 cccttcacca tcgaggacat agaagtcgca ccccccaagg cccatgaagt tcgaattaag 120 atggtggcca ctggtgtctg ccgctcagac gatcacgtgg ttagtggaac cctggtcaca 180

cctcttcctg cagttttagg ccatgaggga gcaggcattg ttgagagcgt tggagaaggg 240

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Lys Ala His Glu Val Arg Ile Lys Met Val Ala Thr Gly Val Cys Arg
Ser Asp Asp His Val Val Ser Gly Thr Leu Val Thr Pro Leu Pro Ala
Val Leu Gly His Glu Gly Ala Gly Ile Val Glu Ser Val Gly Glu Gly
                     70
Val Thr Cys Val Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Ser Pro
                 85
                                     90
Gln Cys Gly Glu Cys Arg Ile Cys Lys His Pro Glu Ser Asn Phe Cys
                                105
                                                    110
Ser Arg Ser Asp Leu Leu Met Pro Arg Gly Thr Leu Arg Glu Gly Thr
Ser Arg Phe Ser Cys Lys Gly Lys Gln Ile His Asn Phe Ile Ser Thr
                        135
Ser Thr Phe Ser Gln Tyr Thr Val Val Asp Asp Ile Ala Val Ala Lys
145
Ile Asp Gly Ala Ser Pro Leu Asp Lys Val Cys Leu Ile Gly Cys Gly
                                    170
Phe Ser Thr Gly Tyr Gly Ser Ala Val Lys Val Ala Lys Val Thr Pro
            180
                                185
                                                     190
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Gly Ser Thr Cys Ala Val Phe Gly Leu Gly Gly Val Gly Leu Ser Val
                            200
Ile Ile Gly Cys Lys Ala Ala Gly Ala Ala Arg Ile Ile Ala Val Asp
                                            220
Ile Asn Lys Asp Lys Phe Ala Lys Ala Lys Glu Leu Gly Ala Thr Glu
Cys Ile Asn Pro Gln Asp Tyr Ser Lys Pro Ile Gln Glu Val Leu Gln
                                    250
Glu Met Thr Asp Gly Gly Val Asp Phe Ser Phe Glu Val Ile Gly Arg
Leu Asp Thr Met Thr Ser Ala Leu Leu Ser Cys His Ala Ala Cys Gly
                            280
Val Ser Val Val Val Gly Val Pro Pro Asn Ala Gln Asn Leu Ser Met
    290
                        295
Asn Pro Met Leu Leu Leu Gly Arg Thr Trp Lys Gly Ala Ile Phe
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                                        315
Gly Phe Lys Ser Lys Asp Ser Val Pro Lys Leu Val Ala Asp Phe
                                    330
Met Ala Lys Lys Phe Pro Leu Asp Pro Leu Ile Thr His Val Leu Pro
Phe Glu Lys Ile Asn Glu Ala Phe Asp Leu Leu Arg Ser Gly Lys Ser
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Ile Arg Thr Val Leu Thr Phe
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                                 25
Lys Ala His Glu Val Arg Ile Lys Met Val Ala Thr Gly Val Cys Arg
Ser Asp Asp His Ala Val Ser Gly Ser Leu Phe Thr Pro Leu Pro Ala
Val Leu Gly His Glu Gly Ala Gly Ile Val Glu Ser Ile Gly Glu Gly
Val Thr Cys Val Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Ser Pro
Gln Cys Gly Lys Cys Arg Ile Cys Lys His Pro Glu Ser Asn Leu Cys
                                105
            100
Cys Gln Thr Lys Asn Leu Thr Gln Pro Lys Gly Ala Leu Leu Asp Gly
                            120
Thr Ser Arg Phe Ser Cys Arg Gly Lys Pro Ile His His Phe Ile Ser
                        135
Thr Ser Thr Phe Ser Gln Tyr Thr Val Val Asp Asp Ile Ala Val Ala
                                         155
Lys Ile Asp Ala Ala Ala Pro Leu Asp Lys Val Cys Leu Ile Gly Cys
                                    170
Gly Phe Ser Thr Gly Tyr Gly Ser Ala Val Gln Val Ala Lys Val Thr
Pro Gly Ser Thr Cys Ala Val Phe Gly Leu Gly Gly Val Gly Leu Ser
                            200
                                                 205
Val Val Ile Gly Cys Lys Thr Ala Gly Ala Ala Lys Ile Ile Ala Val
    210
                        215
                                             220
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1131

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Asp Ile Asn Lys Asp Lys Phe Ala Lys Ala Lys Glu Leu Gly Ala Thr
225
Asp Cys Ile Asn Pro Gln Asp Tyr Thr Lys Pro Ile Gln Glu Val Leu
Gln Glu Met Thr Asp Gly Gly Val Asp Phe Ser Phe Glu Val Ile Gly
                                265
Arg Leu Asp Thr Met Thr Ser Ala Leu Leu Ser Cys His Ser Ala Cys
                            280
Gly Val Ser Val Ile Val Gly Val Pro Pro Ser Ala Gln Ser Leu Ser
                        295
Val Asn Pro Met Ser Leu Leu Gly Arg Thr Trp Lys Gly Ala Ile
                    310
                                        315
Phe Gly Gly Phe Lys Ser Lys Asp Ala Val Pro Lys Leu Val Ala Asp
Phe Met Ala Lys Lys Phe Pro Leu Glu Pro Leu Ile Thr His Val Leu
Pro Phe Glu Lys Ile Asn Glu Ala Phe Asp Leu Leu Arg Ala Gly Lys
                            360
Ser Ile Arg Thr Val Leu Thr Phe
    370
<210> 49
<211> 582
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<213> Homo sapiens
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<223> acylphosphatase
<220>
<221> modified base
<222> (582)
<223> n = g, a, c or t
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cagatttttg aatgttatat atattacctg tatgatggaa ggattaccac tgtacacaaa 540
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Lys Leu Gly Leu Val Gly Trp Val Gln Asn Thr Asp Arg Gly Thr Val
                             40
Gln Gly Gln Leu Gln Gly Pro Ile Ser Lys Val Arg His Met Gln Glu
Trp Leu Glu Thr Arg Gly Ser Pro Lys Ser His Ile Asp Lys Ala Asn
                     70
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Phe Asn Asn Glu Lys Val Ile Leu Lys Leu Asp Tyr Ser Asp Phe Gln
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Ile Val Lys
<210> 51
<211> 640
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<213> Mus musculus
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taagttattt tggttgcatg ttggaaaagt taccacgtat tacaagtatg atgaaataca 600
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<213> Mus musculus
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25

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Ile	Tyr 50	Gly	Asn	Glu	Pro	Glu 55	Ile	Gly	Glu	Ala	Leu 60	Lys	Glu	Asp	Val
Gly 65	Pro	Gly	Lys	Ala	Val 70	Pro	Arg	Glu	Glu	Leu 75	Phe	Val	Thr	Ser	Lys 80
Leu	Trp	Asn	Thr	Lys 85	His	His	Pro	Glu	Asp 90	Val	Glu	Pro	Ala	Leu 95	Arg
Lys	Thr	Leu	Ala 100	Asp	Leu	Gln	Leu	Glu 105	Tyr	Leu	Asp	Leu	Tyr 110	Leu	Met
His	Trp	Pro 115	Tyr	Ala	Phe	Glu	Arg 120	Gly	Asp	Asn	Pro	Phe 125	Pro	Lys	Asn
Ala	Asp 130	Gly	Thr	Ile	Cys	Tyr 135	Asp	Ser	Thr	His	Tyr 140	Lys	Glu	Thr	Trp
Lys 145	Ala	Leu	Glu	Ala	Leu 150	Val	Ala	Lys	Gly	Leu 155	Val	Gln	Ala	Leu	Gly 160
Leu	Ser	Asn	Phe	Asn 165	Ser	Arg	Gln	Ile	Asp 170	Asp	Ile	Leu	Ser	Val 175	Ala
Ser	Val	Arg	Pro 180	Ala	Val	Leu	Gln	Val 185	Glu	Cys	His	Pro	Tyr 190	Leu	Ala
		195					200					205	Glu		
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Tyr	Gly	Arg	Ser	Pro 245	Ala	Gln	Ile	Leu	Leu 250	Arg	Trp	Gln	Val	Gln 255	Arg
-			260					265					Ile 270		
Asn	Ile	Lys 275	Val	Phe	Asp	Phe	Thr 280	Phe	Ser	Pro	Glu	Glu 285	Met	Lys	Gln
Leu	Asn 290	Ala	Leu	Asn	Lys	Asn 295	Trp	Arg	Tyr	Ile	Val 300	Pro	Met	Leu	Thr
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Ile Gly Leu Gly Thr Trp Lys Ser Glu Pro Gly Gln Val Lys Ala Ala
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Ile Lys His Ala Leu Ser Ala Gly Tyr Arg His Ile Asp Cys Ala Ser
Val Tyr Gly Asn Glu Thr Glu Ile Gly Glu Ala Leu Lys Glu Ser Val
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Gly Ser Gly Lys Ala Val Pro Arg Glu Glu Leu Phe Val Thr Ser Lys 70 75 Leu Trp Asn Thr Lys His His Pro Glu Asp Val Glu Pro Ala Leu Arg 90 Lys Thr Leu Ala Asp Leu Gln Leu Glu Tyr Leu Asp Leu Tyr Leu Met 105 His Trp Pro Tyr Ala Phe Glu Arg Gly Asp Asn Pro Phe Pro Lys Asn 120 Ala Asp Gly Thr Val Arg Tyr Asp Ser Thr His Tyr Lys Glu Thr Trp Lys Ala Leu Glu Val Leu Val Ala Lys Gly Leu Val Lys Ala Leu Gly 155 150 Leu Ser Asn Phe Asn Ser Arg Gln Ile Asp Asp Val Leu Ser Val Ala 165 Ser Val Arg Pro Ala Val Leu Gln Val Glu Cys His Pro Tyr Leu Ala 185 Gln Asn Glu Leu Ile Ala His Cys His Ala Arg Gly Leu Glu Val Thr Ala Tyr Ser Pro Leu Gly Ser Ser Asp Arg Ala Trp Arg His Pro Asp Glu Pro Val Leu Leu Glu Glu Pro Val Val Leu Ala Leu Ala Glu Lys His Gly Arg Ser Pro Ala Gln Ile Leu Leu Arg Trp Gln Val Gln Arg 250 Lys Val Ile Cys Ile Pro Lys Ser Ile Asn Pro Ser Arg Ile Leu Gln Asn Ile Gln Val Phe Asp Phe Thr Phe Ser Pro Glu Glu Met Lys Gln 280 Leu Asp Ala Leu Asn Lys Asn Trp Arg Tyr Ile Val Pro Met Ile Thr 295 290 Val Asp Gly Lys Arg Val Pro Arg Asp Ala Gly His Pro Leu Tyr Pro

Phe Asn Asp Pro Tyr 325

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<213> Rattus norvegicus

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             2.0
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Ile Lys Tyr Ala Leu Ser Val Gly Tyr Arg His Ile Asp Cys Ala Ser
Val Tyr Gly Asn Glu Thr Glu Ile Gly Glu Ala Leu Lys Glu Ser Val
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                                             60
Gly Ala Gly Lys Ala Val Pro Arg Glu Glu Leu Phe Val Thr Ser Lys
Leu Trp Asn Thr Lys His His Pro Glu Asp Val Glu Pro Ala Val Arg
Lys Thr Leu Ala Asp Leu Gln Leu Glu Tyr Leu Asp Leu Tyr Leu Met
His Trp Pro Tyr Ala Phe Glu Arg Gly Asp Asn Pro Phe Pro Lys Asn
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Lys Ala Leu Glu Ala Leu Val Ala Lys Gly Leu Val Lys Ala Leu Gly
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Leu Ser Asn Phe Ser Ser Arg Gln Ile Asp Asp Val Leu Ser Val Ala
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                                     170
Ser Val Arg Pro Ala Val Leu Gln Val Glu Cys His Pro Tyr Leu Ala
Gln Asn Glu Leu Ile Ala His Cys Gln Ala Arg Gly Leu Glu Val Thr
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Ala Tyr Ser Pro Leu Gly Ser Ser Asp Arg Ala Trp Arg His Pro Asp
                        215
Glu Pro Val Leu Leu Glu Glu Pro Val Val Leu Ala Leu Ala Glu Lys
225
                    230
His Gly Arg Ser Pro Ala Gln Ile Leu Leu Arg Trp Gln Val Gln Arg
                                    250
Lys Val Ile Cys Ile Pro Lys Ser Ile Thr Pro Ser Arg Ile Leu Gln
Asn Ile Gln Val Phe Asp Phe Thr Phe Ser Pro Glu Glu Met Lys Gln
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Leu Asp Ala Leu Asn Lys Asn Trp Arg Tyr Ile Val Pro Met Ile Thr
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Glu Thr Leu Glu Glu Leu Asp Trp Cys Leu Asp Gln Leu Glu Thr Ile
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Gln Thr Tyr Arg Ser Val Ser Glu Met Ala Ser Asn Lys Phe Lys Arg 65 70 75 80

Met Leu Asn Arg Glu Leu Thr His Leu Ser Glu Met Ser Arg Ser Gly 85 90 95

Asn Gln Val Ser Glu Tyr Ile Ser Asn Thr Phe Leu Asp Lys Gln Asn 100 105 110

Asp Val Glu Ile Pro Ser Pro Thr Gln Lys Asp Arg Glu Lys Lys 115 120 125

Lys Gln Gln Leu Met Thr Gln Ile Ser Gly Val Lys Lys Leu Met His 130 135 140

Ser Ser Ser Leu Asn Asn Thr Ser Ile Ser Arg Phe Gly Val Asn Thr 145 150 155 160

Glu Asn Glu Asp His Leu Ala Lys Glu Leu Glu Asp Leu Asn Lys Trp
165 170 175

Gly Leu Asn Ile Phe Asn Val Ala Gly Tyr Ser His Asn Arg Pro Leu 180 185 190

Thr Cys Ile Met Tyr Ala Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr

Phe Arg Ile Ser Ser Asp Thr Phe Ile Thr Tyr Met Met Thr Leu Glu 210 215 220

Asp His Tyr His Ser Asp Val Ala Tyr His Asn Ser Leu His Ala Ala 225 230 235 240

Asp Val Ala Gln Ser Thr His Val Leu Leu Ser Thr Pro Ala Leu Asp 245 250 255

Ala Val Phe Thr Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala Ala Ala 260 265 270

Ile His Asp Val Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn 275 280 285

Thr Asn Ser Glu Leu Ala Leu Met Tyr Asn Asp Glu Ser Val Leu Glu 290 295 300

Asn His His Leu Ala Val Gly Phe Lys Leu Gln Glu Glu His Cys 305 310 315 320

Asp Ile Phe Met Asn Leu Thr Lys Lys Gln Arg Gln Thr Leu Arg Lys 325 330 335

Met Val Ile Asp Met Val Leu Ala Thr Asp Met Ser Lys His Met Ser 340 345 350

Leu Leu Ala Asp Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser 355 360 365

Ser Gly Val Leu Leu Leu Asp Asn Tyr Thr Asp Arg Ile Gln Val Leu 370 375 380

Arg Asn Met Val His Cys Ala Asp Leu Ser Asn Pro Thr Lys Ser Leu 385 390 395 400

Glu Leu Tyr Arg Gln Trp Thr Asp Arg Ile Met Glu Glu Phe Phe Gln 405 410 415

Gln Gly Asp Lys Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys 420 425 430

Asp Lys His Thr Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp 435 440 445

Tyr Ile Val His Pro Leu Trp Glu Thr Trp Ala Asp Leu Val Gln Pro 450 455 460

Asp Ala Gln Asp Ile Leu Asp Thr Leu Glu Asp Asn Arg Asn Trp Tyr 465 470 475 480

Gln Ser Met Ile Pro Gln Ser Pro Ser Pro Pro Leu Asp Glu Gln Asn 485 490 495

Arg Asp Cys Gln Gly Leu Met Glu Lys Phe Gln Phe Glu Leu Thr Leu 500 505 510

Asp Glu Glu Asp Ser Glu Gly Pro Glu Lys Glu Gly Glu Gly His Ser
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<213> Mus musculus

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Met Ser Tyr Leu Gly Pro Gln Met His Val Asn Leu Ala Ser Ala Pro 100 105 110

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Phe Tyr Tyr Phe Ala Leu Glu Ala Ile Cys Tyr Ile Leu Phe Glu Lys 210 215 220

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Thr Tyr Gly Ile Phe Ile Ala Gln Gly Glu Gln Trp Tyr His Leu Arg
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                                             60
Gln Ala Leu Lys Gln Arg Leu Leu Lys Pro Asp Glu Ala Ala Leu Tyr
Thr Asp Ala Leu Asn Glu Val Ile Ser Asp Phe Ile Thr Arg Leu Asp
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                                     90
Gln Val Arg Ala Glu Ser Glu Ser Gly Asp Gln Val Pro Asp Met Ala
            100
                                105
His Leu Leu Tyr His Leu Ala Leu Glu Ala Ile Thr Tyr Ile Leu Phe
                                                 125
Glu Lys Arg Ile Gly Cys Leu Lys Pro Ser Ile Pro Glu Asp Thr Ala
Ala Phe Ile Arg Ser Val Ala Ile Met Phe Gln Asn Ser Val Tyr Ile
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Thr Phe Leu Pro Lys Trp Thr Arg Pro Leu Leu Pro Phe Trp Lys Arg
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Phe Leu Gln Arg Gln 435

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Thr Gly Gln Asp Arg Pro Arg Leu Arg Ser Leu Ala Glu Leu Pro Gly
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Ala	Pro	Leu 115	Leu	Glu	Gln	Val	Met 120	Arg	Gln	Glu	Gly	Lys 125	Tyr	Pro	Ile
Arg	Asp 130	Ser	Met	Glu	Gln	Trp 135	Lys	Glu	His	Arg	Asp 140	His	Lys	Gly	Leu
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His	Ser	Leu	Asn	Gln 165	Arg	Met	Leu	Lys	Pro 170	Ala	Glu	Ala	Ala	Leu 175	Tyr
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Glu 225	Lys	Arg	Val	Gly	Cys 230	Leu	Glu	Pro	Ser	Ile 235	Pro	Glu	Asp	Thr	Ala 240
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Gly Arg Arg Ile Ala Glu Leu Glu Met Gln Leu Leu Ser Arg Leu
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His Met Glu Asp Phe Thr Pro Phe Pro Gly Thr Glu Ile Asn Phe Leu
Gly Thr Thr His Arg Pro Pro Asn Leu Ala Leu Pro Ser Asn Gly Ser
Met His Gly Tyr Cys Pro Gln Gln Thr Lys Ile Thr Thr Ala Phe Lys
Tyr Ile Asn Thr Val Ile Ser Cys Thr Ile Phe Ile Val Gly Met Val
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Gln Leu Leu Pro Leu Gly Gly Gly Arg Asp Arg Lys Val Arg Asp Leu
Gln Glu Ala Asp Leu Asp Leu Leu Arg Val Thr Leu Ser Ser Lys Pro
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Gln Ala Leu Ala Thr Pro Asn Lys Glu Glu His Gly Lys Arg Lys Lys
Lys Gly Lys Gly Leu Gly Lys Lys Arg Asp Pro Cys Leu Arg Lys Tyr
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           100
Lys Asp Phe Cys Ile His Gly Glu Cys Lys Tyr Val Lys Glu Leu Arg
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Gly Leu Ser Leu Pro Val Glu Asn Arg Leu Tyr Thr Tyr Asp His Thr
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Thr Ile Leu Ala Val Val Ala Val Val Leu Ser Ser Val Cys Leu Leu
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Val Ile Val Gly Leu Leu Met Phe Arg Tyr His Arg Arg Gly Gly Tyr
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2360

205

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Gln Leu Leu Pro Thr Gly Gly Asp Arg Ala Gln Gly Val Gln Asp Leu
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Glu Gly Thr Asp Leu Asn Leu Phe Lys Val Ala Phe Ser Ser Lys Pro
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Gln Gly Leu Ala Thr Pro Ser Lys Glu Arg Asn Gly Lys Lys Lys Lys
Lys Gly Lys Gly Leu Gly Lys Lys Arg Asp Pro Cys Leu Arg Lys Tyr
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Lys Asp Tyr Cys Ile His Gly Glu Cys Arg Tyr Leu Gln Glu Phe Arg
Thr Pro Ser Cys Lys Cys Leu Pro Gly Tyr His Gly His Arg Cys His
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- Leu Tyr Glu Val Met Leu Lys Cys Trp His Pro Lys Ala Glu Met Arg 1315 1320 1325
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Gln 465	Phe	Leu	Pro	Gly	Gly 470	Ser	Met	Cys	Arg	Gly 475	Lys	Thr	Ser	Glu	Cys 480
Asp	Val	Pro	Glu	Tyr 485	Cys	Asn	Gly	Ser	Ser 490	Gln	Phe	Cys	Pro	Pro 495	Asp
Val	Phe	Ile	Gln 500	Asn	Gly	Tyr	Pro	Cys 505	Gln	Asn	Ser	Lys	Ala 510	Tyr	Cys
Tyr	Asn	Gly 515	Met	Cys	Gln	Tyr	Tyr 520	Asp	Ala	Gln	Cys	Gln 525	Val	Ile	Phe
Gly	Ser 530	Lys	Ala	Lys	Ala	Ala 535	Pro	Arg	Asp	Cys	Phe 540	Ile	Glu	Val	Asn
Ser 545	Lys	Gly	Asp	Arg	Phe 550	Gly	Asn	Cys	Gly	Phe 555	Ser	Gly	Ser	Glu	Tyr 560
Lys	Lys	Cys	Ala	Thr 565	Gly	Asn	Ala	Leu	Cys 570	Gly	Lys	Leu	Gln	Cys 575	Glu
Asn	Val	Gln	Asp 580	Met	Pro	Val	Phe	Gly 585	Ile	Val	Pro	Ala	Ile 590	Ile	Gln
Thr	Pro	0		~ 7	_										
		595	Arg	GIÀ	Thr	Lys	Cys 600	Trp	Gly	Val	Asp	Phe 605	Gln	Leu	Gly
Ser	Asp 610	595					600					605			
		595 Val	Pro	Asp	Pro	Gly 615	600 Met	Val	Asn	Glu	Gly 620	605 Thr	Lys	Cys	Asp
Ala 625	610	595 Val Lys	Pro Ile	Asp Cys	Pro Arg 630	Gly 615 Asn	600 Met Phe	Val Gln	Asn Cys	Glu Val 635	Gly 620 Asn	605 Thr Ala	Lys Ser	Cys Val	Asp Leu 640
Ala 625 Asn	610 Gly	595 Val Lys Asp	Pro Ile Cys	Asp Cys Asp 645	Pro Arg 630 Ile	Gly 615 Asn Gln	600 Met Phe Gly	Val Gln Lys	Asn Cys Cys 650	Glu Val 635 His	Gly 620 Asn Gly	605 Thr Ala His	Lys Ser Gly	Cys Val Val 655	Asp Leu 640 Cys
Ala 625 Asn Asn	610 Gly Tyr	595 Val Lys Asp	Pro Ile Cys Lys	Asp Cys Asp 645 Asn	Pro Arg 630 Ile Cys	Gly 615 Asn Gln His	600 Met Phe Gly Cys	Val Gln Lys Glu 665	Asn Cys Cys 650 Asp	Glu Val 635 His	Gly 620 Asn Gly	605 Thr Ala His	Lys Ser Gly Pro	Cys Val Val 655	Asp Leu 640 Cys
Ala 625 Asn Asn Cys	Gly Tyr Ser	595 Val Lys Asp Asn Thr	Pro Ile Cys Lys 660 Lys	Asp Cys Asp 645 Asn	Pro Arg 630 Ile Cys	Gly 615 Asn Gln His	600 Met Phe Gly Cys Gly 680	Val Gln Lys Glu 665 Ser	Asn Cys Cys 650 Asp	Glu Val 635 His Gly	Gly 620 Asn Gly Trp	605 Thr Ala His Ala Gly 685	Lys Ser Gly Pro 670	Cys Val Val 655 Pro	Asp Leu 640 Cys His

Asp Glu Leu Arq Lys Thr Phe Arg Lys Lys Arg Ser Gln Met Ser Asp 725 730 Gly Arg Asn Gln Ala Asn Val Ser Arg Gln Pro Gly Asp Pro Ser Ile Ser Arg Pro Pro Gly Gly Pro Asn Val Ser Arg Pro Pro Gly Gly Pro Gly Val Ser Arg Pro Pro Gly Gly Pro Gly Val Ser Arg Pro Pro Gly 775 Gly Pro Gly Val Ser Arg Pro Pro Pro Gly His Gly Asn Arg Phe Pro Val Pro Thr Tyr Ala Ala Lys Gln Pro Ala Gln Phe Pro Ser Arg Pro 810 Pro Pro Pro Gln Pro Lys Ile Ser Ser Gln Gly Asn Leu Ile Pro Ala Arg Pro Ala Pro Ala Pro Pro Leu Tyr Ser Ser Leu Thr 840 <210> 113 <211> 6 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: hexahistidine (His) affinity tag <400> 113 His His His His His 1 <210> 114 <211> 200 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence:poly-Gly flexible linker <220> <221> MOD RES <222> (6)..(200) <223> Gly residues from position 6 to 200 may be present or absent <400> 114